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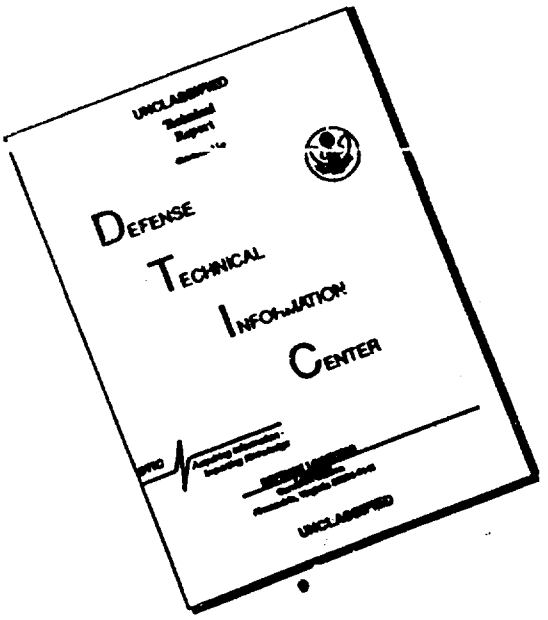

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#137

Journal of Microbiology, Epidemiology and Immunobiology, No. 10, 1955; 83-86.

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On the History of Vaccination against Tularemia.

Seventy years ago N. A. Gaiskii was born. A noted Soviet Scienist who began his work early. He took an early part in anti-plague work, adding to it throughout his life.

One particularly great service of his was the preparation of an anti-tularemia vaccine(live), appreciatively high in anti-epidemic properties content.

Work on the anti-tularemia vaccine was began in the USSR in 1931 by Khatenever and Levchenko and Sinai. They prepared a glycerine vaccine on killed tularemia bacteria. Later Khatenever tested the heated, formalinized vaccines and others. Tests were conducted on guinea pigs. According to Khatenever, the Quinosol vaccine was the most effective.

In 1931 Khatenever was the first im the workto vaccinate humans against tularemia. Forty-one people were vaccinated with a glycerine vaccine. Unfortunately, the vaccinated were under observation for only three weeks.

In 1934 Miller and Grzhebina occupied themselves with the study of tularemia vaccines. They vaccinated rabbits, gophers and white mice with live and killed (agar and glycerine) vaccines. Upon a subsequent infection of these animals a majority of them died.

In 1935 Sinai tested the protective properties of heated glycerine vaccine on white mice, but single, or quadruple immunizations did not protect them from death.

In 1936 Khatenever and Levchenko prepared a vaccine from live, weakly virulent cultures and a polivalent vaccine from killed cultures of B. Tularense. The live, weakly virulent strains were poorly effective and allowed death in a majority of the animals upon infection. The polivalent vaccine, according to Khatenever, gave better results.

In 1937 Miller and Grshebina reported on the local immunization against tularemia by the skin method, for which they used a partially lysed culture, soda and water antigens. The authors concluded that this method increased the resistance of the organism.

Khatenever, and then Burgasov under his supervision, immunized rabbits with a therme-extract. According to the author a just majority of the rabbits survived.

Tests were made on the use of serums from immunized animals, but according to Miller and Grshebina the serums proved weak in a prophylactic sense.

Along with the study of the killed tularemia vaccines there were vaccinations of a small group of humans. Grshebina vaccinated 46 rats with a formalinized vaccine, but 22 of them quickly died. Gerbunov used a polivalent vaccine on 9 workers of the lab. The results were insignificant, 4 of them quickly became ill. Only in one case did Khatenever note good results during the use of a killed tularemia vaccine. In 1944, 598 people of the Tyumensk region were vaccinated,. after 4-5 months none of them became ill with tularemia.

In foreign countries work along this same line was being conducted. Francis (USA) tested formaline and phenol vaccines. He used sub-lethal doses of tularemia cultures and vaccines of avirulent cultures. The tests gave poor results. Filtrates of virulent cultures gave no positive results.

Aaki, Kondo and Tazawa (Japan, 1927-1928) immunised rabbits and guinea pigs with a suspension of brain from dead animals. The suspension was first heated to 60C for 15 minutes. According to them the results were good.

M. Endo (Japan 1930 and 1934) used a heated phenol and formaline vaccine and noted the survival of white mice and guinea pigs upon infection with B. tularense. He prepared the vaccine from avirulent strains.

In 1932 Downs prepared a vaccine with the addition of 0,2% formaline to a suspension of microbes in a physiological solution. The vaccinations were given 6-8times. The animals lived,but were ill for periods up to 90 days.

Oz and Talai Vasfi (Turkey, 1940) immunised animals with a safe endotoxin.

Gotshlich, Galem Sand Bilal and Tansin Berkin (Turkey 1940) used vaccines of live, weaky strains of tularemia. More than 1/3 of the immunised pigs died from the action of the endotoxin, Almost half of the mice died from the tularemia process, the remaining animals survived a subsequent infection.

Foshay, Hesselbrock, Wittenberg and Rodenberg (USA 1942) prepared a vaccine from virulent strains of B. tularense, worked with a water solution of sodium nitrate and acetic acid. Although this was considered to be a most effective vaccine in the USA, its results were not long lasting or very definate, it did not fully protect the vaccinated person.

Madull, Reames, Coriell and Foshay (USA 1950) used phenol and acetone extracts of B. tularense. This vaccine was rated 2/3 effective.

Our survey of all Soviet and foreign literature indicates that the vaccines prepared from killed cultures of B. tularense are ineffective. They required upto 8 applications, and this did not insure a stable, long lasting protection.

The same difficulty was at first experienced with live cultures, this was because the strains were not of a weak virulence and did not possess high immunogenic qualities.

Specific prophylactics against tularemia were more recently developed by N. A. Gaiskii, who, since 1935, together with B. Y. Elbert, conducted studies on tularemia immunity. They found an abd strain of B. tularense with a weak virulence, but with high immunogenic properties (Moscow strain). This strain was tested on 10 volunteers and proven harmless. At the same time it built up antibodies in the organism. This strain was lost, and only in 1941 did Gaiskii find a substitute. One of the weak strains, virulent for white mice and avirulent for guinea pigs, was named 'Bulonnii No. 15, the second-- Ondatra IV dry.'..

Further work on the characteristics of strains of B. Tularense was done by Faibich, Maiskii, Emelyanov and others.

Gaiskii used his weak strains for the preparation of live tularemia vaccines also. In 1942 the first liquid live tularemia vaccine for subcutaneous injection was prepared (called Virus-vaccine).

This vaccine was tested on 50 humans in 1942, 6 people acted as control. All were workers in the anti-plague lab and volunteers.

These tests confirmed the effectiveness and harmlessness of the vaccine. In 1942 1300 people were vaccinated, in 1943-4214 people. This was the first attempt at mass vaccination against tularemia.

The Gaiskii vaccine had good anti-epidemic properties, but had one deficiency, it quickly deteriated at room temperature. This was bad for shipping and sterage.

In 1944 Gaiskii prepared a dry tularemia vaccine. It survived 5 months at 0-2 C. He never finished his work.

Faibich continued Gaiskii's work on the dry vaccine. Using a high vacuum to dry a frozen suspension in a special medium.

Faibich and Tamarin prepared a live dry tularemia vaccine for subcutanteous and cutaneous use. This vaccine survived for two years at a cool temperature. This vaccine is considered as one of the best.

In 1945 Elbert continued a study of the cutaneous method of vaccination. He prepared, together with Tinker, Pushkov and others, a live liquid tularemia vaccine, which allowed for the quick vaccination of large numbers of people.

The on-skin method of vaccination also allowed for the quick detection of immunity. The average skin reaction takes place in 10-15 days. Some reactions are in as little as 2 days, and some 20 days.

Kosmachevski noted other ractions during the introduction of the live vaccine (rise in temperature in 50%, enlarged lymphatic nodes in 30%, etc.). Gaiskii and Khishinskaya noted appearances in 20-40% of all those vaccinated.

The vaccination against tularemia causes the formation of a reaction which can be used to detect the degree of immunity, in many cases 8 years later.

Agglutinins in the blood form after 2-4 weeks, and can be detected for 3-5 years. A shorter lenght of time than the allergic reactions.

Elbert observed that no infections with tularemia took place among those vaccinated, among the non vaccinated the rate was 4.3%

Since 1946 the live tularemia vaccine is used extensively for the prevention of epidemics. It has proven very effective if the vaccinations can be started with in 3-5 days after the initial start of infections. Thus, both the liquid and dry vaccines can be used, both are very effective.

Observations of health workers (those in contact with tularemia) who had been vaccinated indicate that not one single case of infection resulted over a 6 year period.

Infection with tulremia of newly vaccinated personnel is rare after the first week. Most of the cases of infection after vaccination (77.3%) are noted in the first week to twelve days, thecthere are from 12-16 days, after which there are very few. This, evidently, is because in the first week the antibodies have not yet been built up to a point of resistance.

The works of various authors list the period of immunity to be from 6 months to 10 years. We believe the average time is 4 yrs., (absence of illness, immunological reaction, no reaction to revaccination.).

Much credit must be given to Gaiskii, Elbert and Fabich for their work in the study of the tularemia vaccines.